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IMPACT OF ELEVATED PCSK9 LEVELS ON REGULATION OF LDL-CHOLESTEROL AFTER STATIN TREATMENT: STUDY WITH DIFFERENT TYPES OF LIPID LOWERING DRUGS

ACC Poster Contributions
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Background: Statins are known to activate proprotein convertase subtilisin/kexin type 9 (PCSK9) gene which may cancel a part of low-density lipoprotein (LDL)-cholesterol lowering effect of statin by degeneration of LDL receptor in vitro. However, few data exist regarding the relationship between serum LDL-cholesterol (C) and PCSK9 levels under intensive LDL-C lowering therapy in clinical settings.

Methods: Total 16 heterozygous familial hypercholesterolemic (FH) patients (11 men, mean age 64.6±7.7 years) were introduced rosuvastatin (20mg/day), ezetimibe (10mg/day), and colestimide (3g/day) alternately as following. Phase 1: Rosuvastatin (20mg/day) (Group 1) or combination of rosuvastatin (10mg) and ezetimibe (10mg) (Group 2) were introduced for 8 weeks after wash-out period. Phase 2: Combination therapy with rosuvastatin (20mg) and ezetimibe (10mg) for another 8 weeks for both groups. Phase 3: Finally, colestimide (3g) was added for final 8 weeks for both groups.

Results: Serum LDL-C levels significantly decreased by 66% from 295±37 to 100±21 mg/dL ($p<0.001$) after combination use of 3 different cholesterol-lowering drugs, whereas serum levels of PCSK9 significantly increased by 86% from 309±66 to 575±130 (ng/mL) ($p<0.001$). Under these conditions, changes in LDL-C levels do not correlate with those in PCSK9 levels when rosuvastatin was included as one of the induced drugs. Importantly, additional use of ezetimibe and colestimide over rosuvastatin significantly caused further reductions in LDL-cholesterol levels without changing serum PCSK9 levels.

Conclusions: These results demonstrate that statin, not LDL-C absorbing inhibitors, treatment can result in increases in PCSK9 levels in clinical settings. This may explain a part of diminished effects of statin on cholesterol lowering. We suggest PCSK9 as an alternative target to further reduce LDL-C when combining with statins.